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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,247	08/14/2006	Tatsuya Nakai	294136US0X PCT	6936

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
CHUI, MEI PING	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
10/22/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/589,247	NAKAI ET AL.	
	Examiner	Art Unit	
	MEI-PING CHUI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/206 and 08/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

The Examiner acknowledges receipt of application number 10/589,247 filed on 08/14/2006. Claims 1-9 are presented for examination on the merits for patentability.

In claim 3, Applicants are advised to adjust the spacing between each word because some words are too closely together, making reading difficult.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

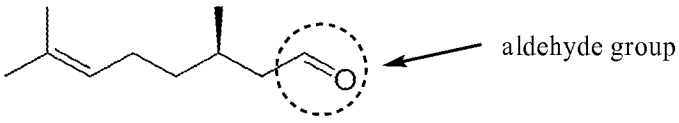
Claims 2, 7, 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) Claim 2 is rejected because it recites the limitation for the ingredient (A) is lovastatin, simvastatin, mevastatin, which R^1 and R^2 groups together form a cyclic lactone, and those recited therein, which represents by the formula (1) according to claim 1. The structure of lovastatin, simvastatin and mevastatin are represented by the compound of formula (1) in that the substituents "R^1 represents an organic residue having a cyclic structure, and R^2 represents a hydrogen or a lower alkyl group". Since claim 1 does not recite the substituents R^1 and R^2

together form a cyclic structure; therefore, the recitation of lovastatin, simvastatin or mevastatin, as claimed in claim 2, lacks antecedent basis.

Claim 2 is also rejected because the name of the ingredient (A) "serivastatin" cannot be found; however, a compound named "cerivastatin" is found. It is unclear the spelling of the compound named "serivastatin" is a typographical error, or Applicants intend to "serivastatin", not "cerivastatin". Clarification is required.

(**2**) Claim 7 is rejected because it recites that "the monocyclic monoterpene having a hydroxyl group is one or more materials selected from menthol, terpineol, and citronellal". However, the structure of citronellal (see below) does not contain a hydroxyl group. It is unclear Applicants intend to include citronellal in the group of linear monoterpene having an aldehyde or in the group of monocyclic monoterpene having a hydroxyl group:



(**3**) Claims 8 and 9 recite the limitations for the amounts of ingredient (A) and monoterpene in % by mass. It is unclear the recited amount, in %, of ingredient (A) and monoterpene are relative to the total weight of the external preparation or they are relative to the weight of the remaining ingredient(s). Therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, and thus rendering the claims indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

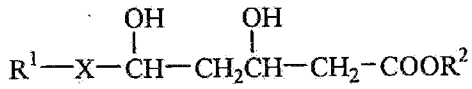
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsuma et al. (EP 0682942 A1).

Applicants Claim

Applicants claim an external preparation comprising an ingredient (A), which is represented by a compound of formula (1), present in 0.001 % to 20 % by mass (see structure below), and a monoterpene which is present in an amount from 0.01 % to 15 % by mass; wherein the compound of formula (1) is atorvastatin, pitavastatin or pravastatin, or the salts thereof, and the monoterpene is menthol, terpineol or citronellal:



,

wherein: **R^1** = an organic residue having a cyclic structure that may have substituents;

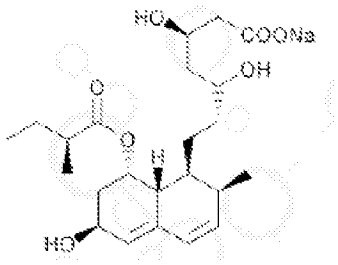
R^2 = a hydrogen atom or a lower alkyl group; and

X = an ethylene group (CH_2CH_2) or an ethenylene group (CH=CH), or a salt thereof.

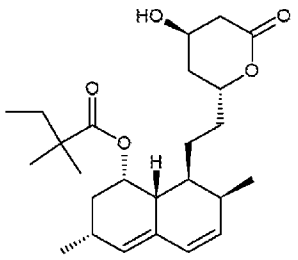
Determination of the scope and content of the prior art
(MPEP 2141.01)

Katsuma et al. teach a novel transdermal therapeutic preparation which can efficiently deliver a pharmaceutically active agent into the living body. Katsuma et al. teach that the transdermal preparation is a highly safe and administration-controllable delivery system in which the transdermal drug absorption-enhancing property of highly safe terpenes is effectively exerted in the delivery system without causing irritation to the skin (page 2, lines 3-5 and 50-54).

Katsuma et al. also teach that the transdermal absorption preparation comprises a pharmaceutically active agent, i.e. simvastatin, pravastatin sodium (see structure below) and the like, which can be used for treating hyperlipemia:



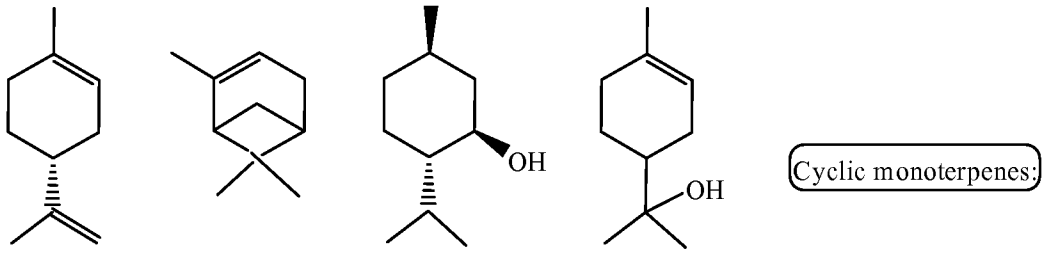
Pravastatin sodium



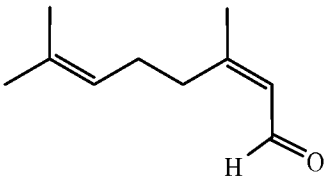
Simvastatin

In addition, Katsuma et al. teach that the active drugs can be used alone or as a mixture of two or more in an amount sufficient to exert desired drug effects (page 5, lines 26 and 36-37).

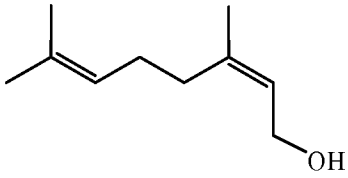
Katsuma et al. teach that the transdermal absorption preparation also comprises a monoterpene or a combination of monoterpenes as transdermal absorption enhancing agent. Katsuma et al. teach that the monoterpene(s) also can be from essential oils, which contain monoterpene(s) as main components (page 3, lines 9 and 20). Katsuma et al. further teach that suitable monoterpene(s), such as those with cyclic hydrocarbon structures, i.e. limonene and pinene; monoterpene(s) with linear structure containing an aldehyde group or a hydroxyl group, i.e. citral or citronellol; monoterpene(s) with cyclic structure containing a hydroxyl group, i.e. menthol and terpineol, are useful as transdermal absorption enhancing agent (page 3, lines 9-20 and 36-40, and structures below):



limonene pinene menthol terpineol



citral



citronellol

Linear monoterpenes:

Furthermore, Katsuma et al. teach that the amount of active drug is present within the range of from 0.01 % to 20 % by weight, based on the weight of the composition, and the amount of monoterpene is present in the range of from 1 % to 50 % by weight, preferably from 1 % to 10 % by weight relative to the weight of the composition (page 3, lines 23-24 and page 5, line 38).

Katsuma et al. then teach that the transdermal absorption preparation is for external purpose (page 5, line 48), in which the external preparation dramatically improves the skin penetration of drugs that are generally considered having relative low skin penetration ability to a great extent (page 21, lines 9-12).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Katsuma et al. teach an external preparation, for drug delivery through transdermal route, comprising a pharmaceutically active agent and a monoterpene, wherein the pharmaceutically active agent can be a hyperlipemia active agent, i.e. simvastatin or pravastatin sodium, and the like; but Katsuma et al. do not explicitly disclose other hyperlipemia active agent, i.e. pitavastatin calcium or atorvastatin calcium as claimed.

Finding of prima facie obviousness Rational and Motivation
(MPEP 2142-2143)

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the guidance of Katsuma et al. to arrive at the instant invention.

One of ordinary skill would have been motivated to select any one of the hyperlipemia agents, i.e. pravastatin, pitavastatin or atorvastatin, and reasonably expect a similar and successful result because they all are active agents that have similar chemical structure and are useful for lowering cholesterol. Thus, they are functional equivalent pharmaceutical drugs, in which any one of them can be used in combination with a monoterpene in a transdermal formulation.

Therefore, the Examiner can only conclude that it is an ordinary innovation to use a monoterpene to deliver a hyperlipemia agent transdermally because the prior art has already suggested doing so. The selection of calcium or sodium salt of the formula (1) as claimed is merely judicious selection and routine optimization that would be dependent on the particular drug selected, the patient and the treatment.

In the absence of evidence to the contrary, it would have been obvious that one of ordinary skill in the art would have had a reasonable expectation of success in producing a formulation for external use, which comprises a mixture of the compound of formula (1) and a monoterpene, as instantly claimed, that performs the same as the transdermal absorption preparation taught in the prior art. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H. C./

Examiner, Art Unit 1616

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616